2521.0115-07

PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	:	Examiner: Not Yet Assigned
MICHAEL D. VARNEY ET AL.	)	
	:	Group Art Unit: N/Y/A
Application No.: CONTINUATION OF 09/782,284	)	
Filed: HEREWITH	)	
For: ANTIPROLIFERATIVE SUBSTITUTED 5-THIAPYRIMIDINONE AND 5-SELENOLYRIMIDINONE COMPOUNDS	)	October 23, 2001

Assistant Commissioner for Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Sir:

Prior to action on the merits, please amend the above-identified application as follows:

IN THE SPECIFICATION:

On Page 1, please delete the first paragraph and insert the following sentence:

—This application is a divisional of allowed U.S. Patent Application No. 09/782,284, filed February 13, 2001, which is a divisional of U.S. Patent Application No.

"Express Mail" mailing label number EH475138556US
Date of Deposit October 23, 2001
I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to: Commissioner for Patents, Washington, D.C. 20231

RAYMOND M. MANDRA
(Typed or printed name of person mailing paper or fee)

(Signature of person mailing paper or fee)

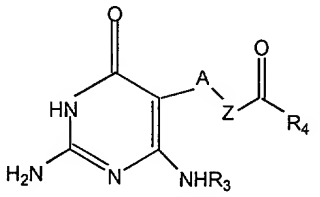
09/588,654, filed June 7, 2000, which is a divisional of U.S. Patent Application No. 09/307,595, filed May 10, 1999, which is a divisional of U.S. Patent Application No. 09/003,163, filed January 6, 1998, now U.S. Patent No. 5,945,427, which is a divisional of U.S. Patent Application No. 08/448,556, filed June 7, 1995, now U.S. Patent No. 5,739,141, which is a 371 of International Application No. PCT/US93/11795, filed December 10, 1993, which is a continuation-in-part of U.S. Patent Application No. 07/991,259, filed December 16, 1992, now abandoned, all of which are incorporated herein by reference.--

IN THE CLAIMS:

Please cancel claims 1-51 without prejudice or disclaimer.

Please insert the following claims 52-61.

52. A compound having the formula V



V

whererin:

A represents sulfur or selenium;

Z represents 1) a substituted or unsubstituted non-cyclic spacer which separates A from the carbonyl carbon of the amido group by 1 to 10 atoms, said atoms being independently selected from carbon, oxygen, sulfur, nitrogen and phosphorous; 2) a substituted or unsubstituted mono- or fused or nonfused poly-carbocyclic or heterocyclic radical; or 3) a combination of at least one of said non-cyclic spacer and at least one of said carbocyclic or heterocyclic radical,

wherein said non-cyclic spacer separates A from one of said carbocyclic or heterocyclic radicals by 1 to 10 atoms;

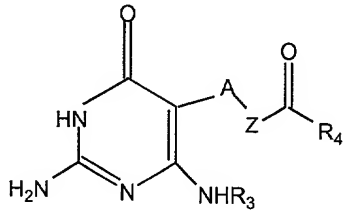
R_3 represents H or a straight, branched or cyclic (C_1 to C_6) alkyl group, optionally carrying one or more hydroxyl or amine groups; and

R_4 represents hydroxy, (C_1 to C_6) alkyloxy group optionally carrying one or more hydroxyl or amine groups, or a protected or unprotected amino acid linked to the acyl group of formula V by the amine portion of the amino acid;

or a pharmaceutically acceptable salt thereof.

53. A compound according to Claim 52 wherein Z represents a substituted or unsubstituted mono- or fused or nonfused poly-heterocyclic radical.

54. A process for preparing a compound having the formula V



V

wherein:

A represents sulfur or selenium;

Z represents 1) a substituted or unsubstituted non-cyclic spacer which separates A from the carbonyl carbon of the amido group by 1 to 10 atoms, said atoms being independently selected from carbon, oxygen, sulfur, nitrogen and phosphorous; 2) a substituted or unsubstituted mono- or fused or nonfused poly-carbocyclic or heterocyclic radical; or 3) a combination of at least one of said non-cyclic spacer and at least one of said carbocyclic or heterocyclic radical,

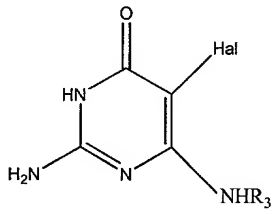
wherein said non-cyclic spacer separates A from one of said carbocyclic or heterocyclic radicals by 1 to 10 atoms;

R_3 represents H or a straight, branched or cyclic (C_1 to C_6) alkyl group, optionally carrying one or more hydroxyl or amine groups; and

R_4 represents hydroxy, (C_1 to C_6) alkyloxy group optionally carrying one or more hydroxyl or amine groups, or a protected or unprotected amino acid linked to the acyl group of formula V by the amine portion of the amino acid;

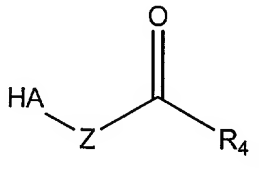
or a pharmaceutically acceptable salt thereof;

which process comprises reacting a compound having the formula VI



VI

wherein Hal is bromine, chlorine, iodine, or fluorine, and R_3 is as defined above, with a compound having the formula IV



IV

wherein A, Z, and R_4 are as defined above, in the presence of a nonnucleophilic auxiliary base in a solvent in which at least one of said reactants is at least partially soluble under conditions sufficient to obtain the compound of formula V.

55. A process according to claim 54 wherein the non-nucleophilic auxiliary

base is selected from alkali or earth metal carbonates and trialkyl amines.

56. A process according to claim 55 wherein the solvent is a dipolar aprotic solvent.

57. A process according to claim 56 wherein the solvent is selected from dimethylsulfoxide, N,N-dimethylformamide, N,N-dimethylacetamide, and N-methyl-2-pyrolidinone.

58. A process according to claim 54 wherein A represents sulfur and Z represents $-(CH_2)_n-X-Ar-$ wherein

n is an integer from 0 to 5,

X represents a methylene, monocyclic carbo- or heterocyclic ring, sulfur, oxygen or amino radical, optionally carrying one or more substituents independently selected from C_1 to C_6 alkyl or C_2 to C_6 alkenyl groups, C_1 to C_6 alkoxy or C_1 to C_6 alkoxy(C_1 to C_6) alkyl groups, C_2 to C_6 alkynyl groups, acyl groups, halogen, amino groups, hydroxyl groups, nitro groups or mercapto groups, monocyclic carbo- or heterocyclic rings, and fused or non-fused poly-carbocyclic or poly-heterocyclic rings; and

Ar represents a monocyclic carbo- or heterocyclic aromatic ring or a bicyclic carbo- or heterocyclic ring, all or a portion of which may be aromatic, and wherein the Ar may be fused to the monocyclic carbo- or heterocyclic ring of X, and wherein the Ar optionally carries one or more substituents independently selected from C_1 to C_6 alkyl or C_2 to C_6 alkenyl groups, C_1 to C_6 alkoxy or C_1 to C_6 alkoxy(C_1 to C_6)alkyl groups, C_2 to C_6 alkynyl groups, acyl groups,

halogen, amino groups, hydroxyl groups, nitro groups or mercapto groups, monocyclic carbo- or heterocyclic rings, and fused or non-fused poly-carbocyclic or poly-heterocyclic rings.

59. A process according to claim 58 wherein the non-nucleophilic auxiliary base is selected from alkali or earth metal carbonates and trialkylamines.

60. A process according to claim 59 wherein the solvent is a dipolar aprotic solvent.

61. A process according to claim 60 wherein the solvent is selected from dimethylsulfoxide, N,N-dimethylformamide, N,N-dimethylacetamide, and N-methyl-2-pyrolidinone.

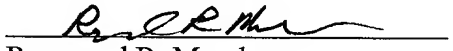
REMARKS

The claims are 52-61.

Support for Claims 52-61 can be found in the Specifications and Claims as originally filed. No new matter has been added. Favorable consideration and early passage to issue is respectfully requested.

Applicants' undersigned attorney may be reached in our New York office by telephone at (212) 218-2100. All correspondence should continue to be directed to our below listed address.

Respectfully submitted,



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